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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,741	11/14/2005	Hiroyuki Aburatani	392.1001	4248

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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,741	ABURATANI ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 10, 2007 is acknowledged and has been entered. Claim 1 has been amended and new claims 23-29 have been added. An action on the RCE follows.

2. Claims 9 and 23-29 are pending and currently under examination.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 9 and 23-29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: complement, peripheral blood mononuclear cells, or an attached toxin that will produce cytotoxic activity against the cell lines HepG2 or Huh-7 when the monoclonal antibody against residues 375-580 of GPC3 is bound to them.

Claim 27 is rejected unde r 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "derived" in claim 27 is also indefinite because there is no art recognized meaning for wherein the V region is" derived" from another antibody. Amendment of the claim to replace "derived" with "obtained" would obviate this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9 and 23-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies **ch.M3C11 and ch.M1E07, wherein the antibody has ADCC activity or CDC activity *in vitro* against the cell line, HepG2 or HUH-7 in the presence of complement or peripheral blood mononuclear cells or when conjugated to a toxin or radioactive materials**, does not reasonably provide enablement for an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, which reads on an antibody with cytotoxic activity in vivo for example for treatment of cancer as contemplated in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and used the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is

required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are broadly drawn to an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7. This means that the claimed monoclonal antibody has cytotoxic activity alone or in combination with other effectors and that the claimed monoclonal antibody has cytotoxic activity *in vitro* or *in vivo*, which reads on an antibody with cytotoxic activity in vivo for example for treatment of cancer as contemplated in the specification.

The specification teaches that the C-terminal peptide of GPC3 is a peptide comprising amino acid residues 359-580 of GPC3 or a peptide comprising amino acid residues 375-580 of GPC3, see p. 4. The specification teaches that antibodies ch.M3C11 and ch.M1E07 to the C-terminus of GPC3 were shown to effectively mediate ADCC (p. 64, 2nd para.) in HepG2 cells and CDC activity (p.67, 2nd para.) in CHO cells overexpressing in *in vitro* assays , wherein either activated PBMC or complement (CHO) was added for the ADCC or CDC, respectively. The specification speculates that if said antibodies are used for treating hepatoma, the antibodies can efficiently reach hepatoma cells without being trapped by the secreted form of GPC3, the N-terminal peptide, present in blood. The specification speculates that such antibodies are useful as agents for disrupting cancer cells and as anticancer agents (p. 68, 2nd para.). Additionally, Aburatani et al. (US Pat App. Pub 20040236080, November 25, 2004) teaches that Huh-7 expresses GPC3

and is susceptible to ADCC and CDC in the presence of monoclonal antibodies to GPC3 and the presence of splenocytes or complement, see Examples 2 and 3 of US Pat App. Pub 20040236080.

Additionally, the specification teaches that the inventors found that an antibody against the C terminus of GPC3 had a high cytotoxic activity and considered that the use of the anti-GPC3 antibody recognizing the C terminus would be preferable for disrupting cancer cell, i.e. for therapeutically treating cancer, see page 3. Furthermore, the specification speculates that because the antibody against the C-terminal peptide of GPC3 in accordance with the invention has a high cytotoxic activity, the antibody can be used for disrupting cancer cells, i.e. for therapeutically treating cancer. Cancer possibly treated clinically using the antibody includes, but is not limited to, hepatoma, pancreatic cancer, lung cancer, colon cancer, breast cancer, prostate cancer, leukemia, and lymphoma. Preferably, the cancer is hepatoma, see paragraph bridging p. 6-7.

One cannot extrapolate the teachings of the specification to enable the scope of the claims because no nexus has been established between an isolated monoclonal antibody against a peptide consisting of amino acid residues of 375-580 of GPC3 as set forth in SEQ ID NO: 4 and cytotoxic activity against HepG2 or Huh-7, except for in the presences of PBMC or complement for ADCC or CDC dependent cytotoxic activity *in vitro*. Furthermore, the art teaches that 1) the mere binding of antibody to its antigen is not predictably sufficient for the induction of cytotoxicity by the antibody and the specification has not shown that any claimed antibody can induce cytotoxicity in the absence of ADCC or CDC and 2) the induction of cytotoxicity against

cell lines in *vivo* is not predictable because the unpredictability of treating tumorigenic cells with antibodies *in vivo* is well known in the art.

1) As drawn to unpredictability of correlating the binding of antibody to an antigen and the induction of cytotoxicity, Young et al. (US Pat. App. Pub 2004/0258693, Dec. 23, 2004) teaches that monoclonal antibody 7BD-33-11A binds to multiple cell lines, but only induced cytotoxicity in a small subset of those cells to which it bound, see Table 1 and 2 and para. 0100-0102. Given the above, in the absence of the teachings in the specification that the claimed monoclonal antibody can stimulate cytotoxicity alone in HepG2 or Huh-7 cells, i.e. in the absence of ADCC or CDC or when conjugated to a toxic agent, undue experimentation would be required to practice the invention as broadly claimed.

2) As drawn to the unpredictability of treating tumorigenic cells with antibodies *in vivo*, as contemplated in the specification, Jain (*Sci. Am.*, 1994, 271:58-65, previously cited), discloses barriers to the delivery of drugs into solid tumors. These impediments include (1) Non-uniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all. (Page 60 col. 3); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61, Col. 1 paragraph 1); (4) Convection is a necessary mechanism by which larger therapeutics molecules such as antibodies, reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors (defined as more than ½ centimeter in diameter, page 62 col. 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of

more than 5000 (page 61, col. 1 through page 63, col. 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform concentration in a tumor that measures 1 centimeter in radius (page 63, col. 2). Curti (*Crit. Rev. in Oncology/Hematology*, 1993, 14:29-39, previously cited) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col. 2). Additionally, Young et al. (US Patent Application Pub. 20040180002, September 15, 2004) teach that there have been many clinical trials of monoclonal antibodies for solid tumors. In the 1980s there were at least 4 clinical trials for human breast cancer, which produced only 1 responder from at least 47 patients using antibodies against specific antigens or based on tissue selectivity. Young et al. teach that It was not until 1998 that there was a successful clinical trial using a humanized anti-her 2 antibody in combination with cisplatin (para 0010 of the published application). The same was true in clinical trials investigating colorectal cancer with antibodies against glycoprotein and glycolipid targets, wherein the specification specifically teaches that "to date there has not been an antibody that has been effective for colorectal cancer. Likewise there have been equally poor results for lung, brain, ovarian, pancreatic, prostate and stomach cancers" (para 0011 of the published

application). Furthermore, Kaiser (Science, 2006, 313, 1370) teaches that 90% of tumor drugs fail in patients, see 3rd col., 2nd to last para.

Additionally, the fact that the antibody is cytotoxic in an *in vitro* system cannot be directly correlated to efficacy in an *in vivo* system as contemplated in the specification. It is well known in the art that many of the factors known to limit human *in vivo* therapeutic efficacy of antibodies are lacking in *in vitro* model environments, for example, the *in vitro* system does not contain molecules that would be expected to proteolytically degrade the antibodies or that would activate an immunological response against the antibodies or that would nonspecifically absorb the antibodies in cells or tissues where the antibody has no effect. Further, it is clear that in the *in vitro* system exemplified, the antibodies are in contact with cells during the entire exposure period. This is not the case *in vivo*, where exposure to the target site may be delayed or inadequate to insure an adequate concentration of the antibodies to be therapeutically effective. Those of skill in the art recognize that *in vitro* assays are useful to screen the effects of agents on cells. However, *in vivo* correlations are generally lacking. For example, Zips et al (In vivo, 2005, 19:1-7) specifically teaches that despite their importance for drug testing, *in vitro* methods are beset by pitfalls and inherent limitations (p. 3, col. 1). In particular the authors state, "It is obvious that cells in culture represent an artificial and simplified system. Unlike the situation *in vitro,* a tumor is a 3-dimensional complex consisting of interacting malignant and non-malignant cells. Vascularisation, perfusion and thereby, drug access to the tumor cells are not evenly distributed and in this fact consists an important source of heterogeneity in tumor response to drugs that does not exist *in vitro.* Therefore, prediction of drug effects in cancer patients based solely on *in vitro* data is not reliable and further evaluations in animal tumor systems is essential"

(p. 3, col. 2). The greatly increased complexity of the *in vivo* environment as compared with the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a simple extrapolation of *in vitro* assays to the *in vivo* environment with any reasonable degree of predictability. Thus, based on the cell culture data presented in the specification, no one of skill in the art would believe it more likely than not that the claimed antibody would function as contemplated in the specification as a anti-cancer therapeutic antibody based only on the cell culture data provided. Thus, undue experimentation would be required to use the invention as contemplated and claimed.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA 1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as claimed or contemplated in the specification based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as claimed or as contemplated in the specification with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

5. Claims 9 and 23-29 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of *wherein the antibody has a cytotoxic activity against the cell line Huh-7*, claimed in claims 9 and 23-29 has no clear support in the specification and the claims as originally filed. Applicants pointed to support for this limitation in the specification in Example 3 and on page 36, line 12 and page 41, line 10. A review of the specification discloses support for detection of the secreted form of GPC3 (Example 3), Huh-7 (page 36, line 12), and HepG2 (page 41, line 10). The suggested support is not found persuasive because there is nothing in the specification to suggest that the monoclonal antibody of claim 9 antibody has a cytotoxic activity against the cell line Huh-7. The subject matter claimed in claims 9 and 25-29 broadens the scope of the invention as originally disclosed in the specification.

6. Claim 9 and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are broadly drawn to an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7.

The state of the art is such that it is well know in the art that it is unpredictable that antibody will have cytotoxic activity against a particular cell in the absence of complement, cytotoxic lymphocytes, or a conjugated toxin. In particular, Young et al. (US Pat. App. Pub 2004/0258693, Dec. 23, 2004) teaches that monoclonal antibody 7BD-33-11A binds to multiple cell lines, but only induced cytotoxicity in a small subset of those cells to which it bound, see Table 1 and 2 and para. 0100-0102. Given the above, in the absence of the teachings in the specification that the claimed monoclonal antibody can stimulate cytotoxicity alone in HepG2 or Huh-7 cells, i.e. in the absence of ADCC or CDC or when conjugated to a toxic agent it is clear that in the antibody arts that an adequate written description is essential for one of skill in the art to make and use the claimed invention.

Given the broadly defined antibody of claim 9, which is required to have cytotoxic activity against HepG2 or Huh-7 cells, it is evident that the specification does not provide a written description of the broadly claimed antibody for the reasons set forth below.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical

species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with

a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7 per Lilly by structurally describing a representative number of isolated monoclonal antibodies against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of an isolated monoclonal antibody against a peptide consisting of amino acid residues

375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, nor does the specification provide any partial structure of such an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, nor any physical or chemical characteristics of an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. The specification does not disclose any isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7, thus it does not provide said antibody that would satisfy the standard set out in Enzo.

The specification also fails to describe an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7 by the test set out in Lilly. The specification does not describes any isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7. Therefore, it necessarily fails to describe a "representative number" of species of an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or

HUH-7. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7that is required to practice the claimed invention or reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the broadly claimed invention.

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

PJR